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     (FILE 'HOME' ENTERED AT 18:33:26 ON 01 AUG 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:34:03 ON 01 AUG
     2002
L1        30967 S PARAMYXOVIRUS OR MORBILLIVIRUS OR RUBULAVIRUS OR
PNEUMOVIRUS
L2       202881 S (REDUC? OR ELIMINAT? OR DECREAS? OR DEMINISH? OR
SUPPRESS?)(8
L3           42 S L1 AND L2
L4        37005 S (MUMPS OR PARAINFLUENZA OR SENDAI OR MEASLES OR
RINDERPEST)(3
L5        62860 S (PHOCINE(W)DISTEMPER OR CANINE OR SIMIAN OR
NEWCASTLE)(3A)VIR
L6            0 S (HUMAN(W)ORESPIRATORY OR BOVINE(W)RESPATORY)(3A)VIRUS
L7         2929 S (HUMAN(W)RESPIRATORY OR BOVINE(W)RESPIRATORY)(3A)VIRUS
L8        99541 S L4 OR L5 OR L7
L9       112591 S L1 OR L8
L10        1227 S L2 AND L8
L11      162483 S (REDUC? OR ELIMINAT? OR DECREAS? OR DEMINISH? OR
SUPPRESS?)(4
L12        1117 S L11 AND L9
L13         492 S L11(S)L8
L14         496 S L11(S)L9
L15      871841 S GFP OR MARKER OR GALACTOSIDASE OR LUCIFERASE
L16          32 S L14 AND L15
L17          15 DUP REM L16 (17 DUPLICATES REMOVED)
L18       73317 S (REDUC? OR ELIMINAT? OR DECREAS? OR DEMINISH?)(4A)(TUMOR OR
C
L19         195 S L9 AND L18
L20          91 S L9(S)L18
L21          41 DUP REM L20 (50 DUPLICATES REMOVED)

=>  d au ti so 1-40 l21

L21  ANSWER 1 OF 41     MEDLINE                          DUPLICATE 1
AU   Hayden Brandy C; Murray Timothy G; Cicciarelli Nicole; Scott Ingrid U;
     Alexandridou Anastassia; Hernandez Eleut; Wu Xiaodong; Markoe Arnold M;
     Feuer William; Fulton Lilia; O'Brien Joan M
TI   Hyperfractionated external beam radiation therapy in the treatment of
     murine transgenic retinoblastoma.
SO   ARCHIVES OF OPHTHALMOLOGY, (2002 Mar) 120 (3) 353-9.
     Journal code: 7706534. ISSN: 0003-9950.

L21  ANSWER 2 OF 41  CAPLUS  COPYRIGHT 2002 ACS
IN   Brennan, Frank
TI   Modified plant viruses and methods of use thereof
SO   PCT Int. Appl., 89 pp.
     CODEN: PIXXD2

L21  ANSWER 3 OF 41  CAPLUS  COPYRIGHT 2002 ACS
IN   Russell, James; Cattaneo, Roberto; Peng, Kah-Whye; Schneider, Urs;
Murphy,
     Anthea L.
TI   Therapeutic methods and compositions using viruses of the recombinant
     Paramyxoviridae family
SO   PCT Int. Appl., 102 pp.
     CODEN: PIXXD2
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L21 ANSWER 4 OF 41 MEDLINE DUPLICATE 2
AU Uchida A; O'Keefe D S; Bacich D J; Molloy P L; Heston W D
TI In vivo suicide gene therapy model using a newly discovered prostate-specific membrane antigen promoter/enhancer: a potential alternative approach to androgen deprivation therapy.
SO UROLOGY, (2001 Aug) 58 (2 Suppl 1) 132-9.
Journal code: 0366151. ISSN: 1527-9995.

L21 ANSWER 5 OF 41 MEDLINE DUPLICATE 3
AU Mikola M K; Rahman N A; Paukku T H; Ahtiainen P M; Vaskivuo T E; Tapanainen J S; Poutanen M; Huhtaniemi I T
TI Gonadal tumors of mice double transgenic for inhibin-alpha promoter-driven simian virus 40 T-antigen and herpes simplex virus thymidine kinase are sensitive to ganciclovir treatment.
SO JOURNAL OF ENDOCRINOLOGY, (2001 Jul) 170 (1) 79-90.
Journal code: 0375363. ISSN: 0022-0795.

L21 ANSWER 6 OF 41 MEDLINE DUPLICATE 4
AU Sereda A D; Gavrilov K E; Fugina L G
TI [Distemper of carnivore: Proliferative activity of lymphocytes in sick and vaccinated dogs].
Chuma plotoiadnykh: Proliferativnaia aktivnost' limfotsitov u bol'nykh i vaktsinirovannykh sobak.
SO VOPROSY VIRUSOLOGII, (1999 Nov-Dec) 44 (6) 257-61.
Journal code: 0417337. ISSN: 0507-4088.

L21 ANSWER 7 OF 41 MEDLINE DUPLICATE 5
AU Martin D C; Sanchez-Sweatman O H; Ho A T; Inderdeo D S; Tsao M S; Khokha R
TI Transgenic TIMP-1 inhibits simian virus 40 T antigen-induced hepatocarcinogenesis by impairment of hepatocellular proliferation and tumor angiogenesis.
SO LABORATORY INVESTIGATION, (1999 Feb) 79 (2) 225-34.
Journal code: 0376617. ISSN: 0023-6837.

L21 ANSWER 8 OF 41 MEDLINE DUPLICATE 6
AU Howard C M; Claudio P P; Gallia G L; Gordon J; Giordano G G; Hauck W W; Khalili K; Giordano A
TI Retinoblastoma-related protein pRb2/p130 and suppression of tumor growth in vivo.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1998 Oct 7) 90 (19) 1451-60.
Journal code: 7503089. ISSN: 0027-8874.

L21 ANSWER 9 OF 41 MEDLINE DUPLICATE 7
AU Cooper M J; Lippa M; Payne J M; Hatzivassiliou G; Reifenberg E; Fayazi B; Perales J C; Morrison L J; Templeton D; Piekarz R L; Tan J
TI Safety-modified episomal vectors for human gene therapy.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Jun 10) 94 (12) 6450-5.
Journal code: 7505876. ISSN: 0027-8424.

L21 ANSWER 10 OF 41 MEDLINE DUPLICATE 8
AU Kananen K; Rilianawati; Paukku T; Markkula M; Rainio E M; Huhtanemi I
TI Suppression of gonadotropins inhibits gonadal tumorigenesis in mice transgenic for the mouse inhibin alpha-subunit promoter/simian virus 40 T-antigen fusion gene.
SO ENDOCRINOLOGY, (1997 Aug) 138 (8) 3521-31.

Journal code: 0375040. ISSN: 0013-7227.

L21 ANSWER 11 OF 41 MEDLINE DUPLICATE 9
AU Plymate S R; Bae V L; Maddison L; Quinn L S; Ware J L
TI Reexpression of the type 1 insulin-like growth factor receptor inhibits the malignant phenotype of simian virus 40 T antigen immortalized human prostate epithelial cells.
SO ENDOCRINOLOGY, (1997 Apr) 138 (4) 1728-35.
Journal code: 0375040. ISSN: 0013-7227.

L21 ANSWER 12 OF 41 MEDLINE DUPLICATE 10
AU Speiser D E; Miranda R; Zakarian A; Bachmann M F; McKall-Faienza K; Odermatt B; Hanahan D; Zinkernagel R M; Ohashi P S
TI Self antigens expressed by solid tumors Do not efficiently stimulate naive
or activated T cells: implications for immunotherapy.
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1997 Aug 29) 186 (5) 645-53.
Journal code: 2985109R. ISSN: 0022-1007.

L21 ANSWER 13 OF 41 MEDLINE DUPLICATE 11
AU Takakuwa K; Fujita K; Kikuchi A; Sugaya S; Yahata T; Aida H; Kurabayashi T; Hasegawa I; Tanaka K
TI Direct intratumoral gene transfer of the herpes simplex virus thymidine kinase gene with DNA-liposome complexes: growth inhibition of tumors and lack of localization in normal tissues.
SO JAPANESE JOURNAL OF CANCER RESEARCH, (1997 Feb) 88 (2) 166-75.
Journal code: 8509412. ISSN: 0910-5050.

L21 ANSWER 14 OF 41 MEDLINE DUPLICATE 12
AU Chakrabarti B K; Maitra R K; Ma X Z; Kestler H W
TI A candidate live inactivatable attenuated vaccine for AIDS.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Sep 3) 93 (18) 9810-5.
Journal code: 7505876. ISSN: 0027-8424.

L21 ANSWER 15 OF 41 MEDLINE DUPLICATE 13
AU Kananen K; Markkula M; Mikola M; Rainio E M; McNeilly A; Huhtaniemi I
TI Gonadectomy permits adrenocortical tumorigenesis in mice transgenic for the mouse inhibin alpha-subunit promoter/simian virus 40 T-antigen fusion gene: evidence for negative autoregulation of the inhibin alpha-subunit gene.
SO MOLECULAR ENDOCRINOLOGY, (1996 Dec) 10 (12) 1667-77.
Journal code: 8801431. ISSN: 0888-8809.

L21 ANSWER 16 OF 41 MEDLINE DUPLICATE 14
AU Sinkovics J G; Horvath J
TI Can virus therapy of human cancer be improved by apoptosis induction?.
SO MEDICAL HYPOTHESES, (1995 May) 44 (5) 359-68. Ref: 72
Journal code: 7505668. ISSN: 0306-9877.

L21 ANSWER 17 OF 41 MEDLINE DUPLICATE 15
AU Warnke P C; Molnar P; Lapin G D; Kuruvilla A; Groothuis D R
TI The effects of dexamethasone on transcapillary transport in experimental brain tumors: II. Canine brain tumors.
SO JOURNAL OF NEURO-ONCOLOGY, (1995) 25 (1) 29-38.
Journal code: 8309335. ISSN: 0167-594X.

L21 ANSWER 18 OF 41 MEDLINE DUPLICATE 16
AU Plaksin D; Porgador A; Vadai E; Feldman M; Schirrmacher V; Eisenbach L
TI Effective anti-metastatic melanoma vaccination with tumor cells

transfected with MHC genes and/or infected with Newcastle disease virus (NDV).
SO INTERNATIONAL JOURNAL OF CANCER, (1994 Dec 15) 59 (6) 796-801.
Journal code: 0042124. ISSN: 0020-7136.

L21 ANSWER 19 OF 41 MEDLINE DUPLICATE 17
AU Sandgren E P; Luetteke N C; Qiu T H; Palmiter R D; Brinster R L; Lee D C
TI Transforming growth factor alpha dramatically enhances oncogene-induced carcinogenesis in transgenic mouse pancreas and liver.
SO MOLECULAR AND CELLULAR BIOLOGY, (1993 Jan) 13 (1) 320-30.
Journal code: 8109087. ISSN: 0270-7306.

L21 ANSWER 20 OF 41 MEDLINE DUPLICATE 18
AU Matozaki T; Sakamoto C; Suzuki T; Matsuda K; Uchida T; Nakano O; Wada K; Nishisaki H; Konda Y; Nagao M; +
TI p53 gene mutations in human gastric cancer: wild-type p53 but not mutant p53 suppresses growth of human gastric cancer cells.
SO CANCER RESEARCH, (1992 Aug 15) 52 (16) 4335-41.
Journal code: 2984705R. ISSN: 0008-5472.

L21 ANSWER 21 OF 41 MEDLINE DUPLICATE 19
AU Leopardi R; Vainionpaa R; Hurme M; Siljander P; Salmi A A
TI **Measles virus** infection enhances IL-1 beta but **reduces tumor** necrosis factor-alpha expression in human monocytes.
SO JOURNAL OF IMMUNOLOGY, (1992 Oct 1) 149 (7) 2397-401.
Journal code: 2985117R. ISSN: 0022-1767.

L21 ANSWER 22 OF 41 MEDLINE DUPLICATE 20
AU Bravard A; Hoffschir F; Sabatier L; Ricoul M; Pinton A; Cassingena R; Estrade S; Luccioni C; Dutrillaux B
TI Early superoxide dismutase alterations during SV40-transformation of human fibroblasts.
SO INTERNATIONAL JOURNAL OF CANCER, (1992 Nov 11) 52 (5) 797-801.
Journal code: 0042124. ISSN: 0020-7136.

L21 ANSWER 23 OF 41 MEDLINE DUPLICATE 21
AU Moore M; Teresky A K; Levine A J; Seiberg M
TI p53 mutations are not selected for in simian virus 40 T-antigen-induced tumors from transgenic mice.
SO JOURNAL OF VIROLOGY, (1992 Feb) 66 (2) 641-9.
Journal code: 0113724. ISSN: 0022-538X.

L21 ANSWER 24 OF 41 MEDLINE DUPLICATE 22
AU Stein L S; Welsh T H Jr; Wilson V G; Burghardt R C
TI Cell-to-cell communication competence in **simian virus** 40-transfected rat ovarian cells is **reduced** following **tumor** selection.
SO IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY, (1992 Jun) 28A (6) 436-44.
Journal code: 8506951. ISSN: 0883-8364.

L21 ANSWER 25 OF 41 MEDLINE DUPLICATE 23
AU St Clair D K; Holland J C
TI Complementary DNA encoding human colon cancer manganese superoxide dismutase and the expression of its gene in human cells.
SO CANCER RESEARCH, (1991 Feb 1) 51 (3) 939-43.
Journal code: 2984705R. ISSN: 0008-5472.

L21 ANSWER 26 OF 41 SCISEARCH COPYRIGHT 2002 ISI (R)

AU STCLAIR D K (Reprint); HOLLAND J C
TI COMPLEMENTARY-DNA ENCODING HUMAN COLON CANCER MANGANESE SUPEROXIDE-DISMUTASE AND THE EXPRESSION OF ITS GENE IN HUMAN-CELLS
SO CANCER RESEARCH, (1991) Vol. 51, No. 3, pp. 939-943.

L21 ANSWER 27 OF 41 MEDLINE DUPLICATE 24
AU Bradl M; Klein-Szanto A; Porter S; Mintz B
TI Malignant melanoma in transgenic mice.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 Jan 1) 88 (1) 164-8.
Journal code: 7505876. ISSN: 0027-8424.

L21 ANSWER 28 OF 41 MEDLINE DUPLICATE 25
AU Lyn-Cook B D; Siegal G P; Kaufman D G
TI Malignant transformation of human endometrial stromal cells by transfection of c-myc: effects of pRSVneo cotransfection and treatment with MNNG.
SO PATHOBIOLOGY, (1990) 58 (3) 146-52.
Journal code: 9007504. ISSN: 1015-2008.

L21 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 26
AU Pancheva, S.
TI Combined effect of glycosylation inhibitors on the Newcastle disease virus
in Erhlich ascites tumor cells
SO Acta Microbiol. Bulg. (1987), 20, 88-93
CODEN: AMBUDI; ISSN: 0204-8809

L21 ANSWER 30 OF 41 MEDLINE DUPLICATE 27
AU Giese N A; Neary K E; Levine N; Lindell T J; Duffy J J
TI Inhibition by retinoic acid of murine retrovirus-induced cellular transformation and tumor formation.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1985 May) 74 (5) 1135-44.
Journal code: 7503089. ISSN: 0027-8874.

L21 ANSWER 31 OF 41 MEDLINE
AU Nakagawa Y; Suzuki K; Ibayashi N; Ueda S; Hirakawa K; Oku T; Imanishi J; Kishida T
TI Effect of interferon on mouse glioma.
SO NO TO SHINKEI. BRAIN AND NERVE, (1983 Nov) 35 (11) 1125-30.
Journal code: 0413550. ISSN: 0006-8969.

L21 ANSWER 32 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AU FUNA K; ALM G V; RONNBLOM L; OBERG K
TI EVALUATION OF THE NATURAL KILLER CELL INTERFERON SYSTEM IN PATIENTS WITH MID GUT CARCINOID TUMORS TREATED WITH LEUKOCYTE INTERFERON.
SO CLIN EXP IMMUNOL, (1983) 53 (3), 716-724.
CODEN: CEXIAL. ISSN: 0009-9104.

L21 ANSWER 33 OF 41 MEDLINE DUPLICATE 28
AU Masuda A; Goshima K
TI The role of extracellular calcium ions in HVJ (Sendai virus)-induced cell fusion.
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1980 Jul) 599 (2) 596-609.
Journal code: 0217513. ISSN: 0006-3002.

L21 ANSWER 34 OF 41 MEDLINE
AU Ohtaki S
TI Suppressive effects on simian virus 40-induced oncogenesis of several immunosuppressive agents and hormonal modifications applied during the

latent period.
SO CANCER RESEARCH, (1978 Dec) 38 (12) 4698-710. Ref: 47
Journal code: 2984705R. ISSN: 0008-5472.

L21 ANSWER 35 OF 41 MEDLINE
AU Henriksen O; Law L W; Appella E
TI Quantitative in vivo studies of soluble simian virus 40 tumor-specific transplantation antigens of the mouse.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1977 Jun) 58 (6) 1785-8.
Journal code: 7503089. ISSN: 0027-8874.

L21 ANSWER 36 OF 41 MEDLINE DUPLICATE 29
AU Peters R L; Sass B; Stephenson J R; Al-Ghazzouli I K; Hino S; Donahoe R M;
Kende M; Aaronson S A; KElloff G J
TI Immunoprevention of x-ray-induced leukemias in the C57BL mouse.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1977 Apr) 74 (4) 1697-701.
Journal code: 7505876. ISSN: 0027-8424.

L21 ANSWER 37 OF 41 MEDLINE
AU Topp W; Hall J D; Marsden M; Teresky A K; Rifkin D; Levine A J; Pollack R
TI In vitro differentiation of teratomas and the distribution of creatine phosphokinase and plasminogen activator in teratocarcinoma-derived cells.
SO CANCER RESEARCH, (1976 Nov) 36 (11 Pt. 2) 4217-23.
Journal code: 2984705R. ISSN: 0008-5472.

L21 ANSWER 38 OF 41 MEDLINE
AU Kuzumaki N; Kobayashi H
TI Reduced transplantability of syngenic mouse tumors superinfected with membrane viruses in nu/nu mice.
SO TRANSPLANTATION, (1976 Dec) 22 (6) 545-50.
Journal code: 0132144. ISSN: 0041-1337.

L21 ANSWER 39 OF 41 MEDLINE
AU Diamandopoulos G T; McLane M F
TI Effect of host age, virus dose, and route of inoculation on tumor incidence, latency, and morphology in Syrian hamsters inoculated intravenously with oncogenic DNA simian virus 40.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1975 Aug) 55 (2) 479-82.
Journal code: 7503089. ISSN: 0027-8874.

L21 ANSWER 40 OF 41 MEDLINE
AU Moolten F L; Capparell N J; Zajdel S H; Cooperband S R
TI Antitumor effects of antibody-diphtheria toxin conjugates. II. Immunotherapy with conjugates directed against tumor antigens induced by simian virus 40.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1975 Aug) 55 (2) 473-7.
Journal code: 7503089. ISSN: 0027-8874.

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L22 3 L21 AND L15

=> d au ti so ab 1-3 l22

L22 ANSWER 1 OF 3 MEDLINE
AU Uchida A; O'Keefe D S; Bacich D J; Molloy P L; Heston W D
TI In vivo suicide gene therapy model using a newly discovered

prostate-specific membrane antigen promoter/enhancer: a potential alternative approach to androgen deprivation therapy.
SO UROLOGY, (2001 Aug) 58 (2 Suppl 1) 132-9.
Journal code: 0366151. ISSN: 1527-9995.
AB Prostate-specific membrane antigen (PSMA) is a type-2 membrane protein expressed in the prostate, and it is highly expressed in metastatic or poorly differentiated adenocarcinomas. Moreover, PSMA expression is upregulated by androgen deprivation. These advantages make PSMA a useful target for prostate cancer therapy, especially in combination with conventional hormonal treatment. We recently reported that a prostate-specific enhancer is present in the third intron of the PSMA gene. In this study, we have further analyzed the activity of PSMA promoter/enhancer in prostate cancer cells and cells of other tissue origins (breast cancer MCF-7, lung cancer H157, and colorectal cancer HCT8
cells), and we have examined whether this construct could be used for efficient expression of the suicide gene, cytosine deaminase (CD), in vivo. The PSMA promoter/enhancer expressed the **luciferase** reporter gene in the prostate cancer lines LNCaP and C4-2, with 8- to 20-fold higher expression than the **simian virus** 40 promoter/enhancer, although it was inactive in the other cell lines. This construct efficiently drove the suicide gene CD, sensitizing C4-2 cells to
5-fluorocytosine (5-FC) with the inhibitory concentration (IC(50)) <300 micromol/L in vitro. Athymic male nude mice bearing the transfected C4-2 cells were treated with intraperitoneal injections of either 5-FC (600 mg/kg) twice a day or saline solution for 3 weeks. C4-2 cell **tumors** were **eliminated** by 5-FC when they were expressing our therapeutic construct carrying CD under the regulatory control of the PSMA promoter/enhancer. Our results show the in vivo utility of the PSMA promoter/enhancer in a gene therapy situation targeting prostate cancer.

L22 ANSWER 2 OF 3 MEDLINE
AU Cooper M J; Lippa M; Payne J M; Hatzivassiliou G; Reifenberg E; Fayazi B; Perales J C; Morrison L J; Templeton D; Piekarz R L; Tan J
TI Safety-modified episomal vectors for human gene therapy.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Jun 10) 94 (12) 6450-5.
Journal code: 7505876. ISSN: 0027-8424.
AB The effectiveness of ongoing gene therapy trials may be limited by the expression characteristics of viral and plasmid-based vectors. To enhance levels of heterologous gene expression, we have developed a safety-modified episomal expression vector that replicates extrachromosomally in human cells. This vector system employs a **simian virus** 40 (SV40) large T antigen mutant (107/402-T) that is deficient in binding to human tumor suppressor gene products, including p53, retinoblastoma, and p107, yet retains replication
competence. These SV40-based episomes replicate to thousands of copies by 2-4 days after gene transfer in multiple types of human cell lines, with lower activity in hamster cells, and no detectable activity in dog, rat, and murine cell lines. Importantly, 107/402-T has enhanced replication activity compared with wild-type T antigen; this finding may be due, in part, to the inability of p53 and retinoblastoma to inactivate 107/402-T function. We demonstrate that the level and duration of 107/402-T expression regulates the observed episomal copy number per cell. Compared with standard plasmid constructs, episomes encoding 107/402-T yield approximately 10- to 100-fold enhanced levels of gene expression in unselected populations of transient transfectants. To determine if 107/402-T-based episomes replicate extrachromosomally in vivo, tumor

explants in nude mice were directly injected with liposome/DNA complexes. Using a PCR-based assay, we demonstrate that SV40-based episomes replicate in human cells after direct in vivo gene transfer. These data suggest that safety-modified SV40-based episomes will be effective for cancer gene therapy because high level expression of therapeutic genes in transient transfectants should yield enhanced **tumor elimination**.

L22 ANSWER 3 OF 3 MEDLINE

AU Takakuwa K; Fujita K; Kikuchi A; Sugaya S; Yahata T; Aida H; Kurabayashi T; Hasegawa I; Tanaka K

TI Direct intratumoral gene transfer of the herpes simplex virus thymidine kinase gene with DNA-liposome complexes: growth inhibition of tumors and lack of localization in normal tissues.

SO JAPANESE JOURNAL OF CANCER RESEARCH, (1997 Feb) 88 (2) 166-75. Journal code: 8509412. ISSN: 0910-5050.

AB To constitute the site-specific expression of the herpes simplex virus thymidine-kinase (HSV-TK) gene in tumor cells, we have assessed the promoter function of the **simian virus** 40 (SV40) promoter and the 5'flanking region of c-erbB-2 gene using a **luciferase**-expressing reporter plasmid. After the transfection of the **luciferase** plasmid directed by the promoter region of c-erbB-2 gene, a large amount of **luciferase** activity was observed in c-erbB-2-expressing cells (Colo201, MCF-7, and HEC1-A), while none was detected in cells with no expression of c-erbB-2 protein (HRA and KF cells). On the other hand, a high level of **luciferase** activity was detected in all tumor cell lines tested, when the transfection was performed with SV40 promoter. The repeated transfection of the liposome-conjugated HSV-TK gene regulated by the SV40 promoter or by the promoter region of c-erbB-2 gene with cultivation in 100 micrograms/ml of aciclovir for 5 days in vitro resulted in growth inhibition for all four cell lines examined or for only c-erbB-2-expressing cells in the presence of SV40 promoter or c-erbB-2 promoter, respectively. Finally, direct injection of the DNA-liposome complex into established tumors in the presence of 50 mg/kg of aciclovir led to significant **tumor** volume **reduction** in all three **tumors** tested when SV40 promoter was employed. However, this anti-tumor effect was noted only in c-erbB-2-positive cells (Colo201 cells) upon intratumoral injection of HSV-TK gene regulated by c-erbB-2 promoter. In the case of intratumoral gene transfer, foreign DNA was detected in only one of seven mice by polymerase chain reaction (PCR) analysis performed 7 days following injection. When PCR analysis was carried out at 14 or 21 days following injection, no DNA signal was found at all. However, DNA was detected in several normal tissues at all three times tested in the case of intravenous injection. No abnormalities were seen in histologic examinations of normal tissues or in serum biochemical parameters following DNA liposome delivery. These results suggest that the direct gene transfer of HSV-TK gene regulated by tumor-specific transcriptional units may be one of the most clinically promising of the selective genetic strategies against cancer.

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     (FILE 'HOME' ENTERED AT 18:33:26 ON 01 AUG 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:34:03 ON 01 AUG
     2002
L1        30967 S PARAMYXOVIRUS OR MORBILLIVIRUS OR RUBULAVIRUS OR
PNEUMOVIRUS
L2       202881 S (REDUC? OR ELIMINAT? OR DECREAS? OR DEMINISH? OR
SUPPRESS?)(8
L3           42 S L1 AND L2
L4        37005 S (MUMPS OR PARAINFLUENZA OR SENDAI OR MEASLES OR
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L5        62860 S (PHOCINE(W)DISTEMPER OR CANINE OR SIMIAN OR
NEWCASTLE)(3A)VIR
L6            0 S (HUMAN(W)0RESPIRATORY OR BOVINE(W)RESPATORY)(3A)VIRUS
L7         2929 S (HUMAN(W)RESPIRATORY OR BOVINE(W)RESPIRATORY)(3A)VIRUS
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L11      162483 S (REDUC? OR ELIMINAT? OR DECREAS? OR DEMINISH? OR
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L13         492 S L11(S)L8
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L15      871841 S GFP OR MARKER OR GALACTOSIDASE OR LUCIFERASE
L16          32 S L14 AND L15
L17          15 DUP REM L16 (17 DUPLICATES REMOVED)
L18       73317 S (REDUC? OR ELIMINAT? OR DECREAS? OR DEMINISH?)(4A)(TUMOR OR
C
L19         195 S L9 AND L18
L20          91 S L9(S)L18
L21          41 DUP REM L20 (50 DUPLICATES REMOVED)
L22           3 S L21 AND L15
L23      251522 S VIRUS(6A)INFECTION
L24      253595 S VIRUS(6A)(INFECTION OR TRANSDUCTION)
L25           9 S L21 AND L24

=> d au ti so ab 1-9 l25

L25  ANSWER 1 OF 9     MEDLINE
AU   Plaksin D; Porgador A; Vadai E; Feldman M; Schirrmacher V; Eisenbach L
TI   Effective anti-metastatic melanoma vaccination with tumor cells
     transfected with MHC genes and/or infected with Newcastle disease virus
     (NDV).
SO   INTERNATIONAL JOURNAL OF CANCER, (1994 Dec 15) 59 (6) 796-801.
     Journal code: 0042124. ISSN: 0020-7136.
AB   The therapeutic efficacy of active immunization with B16-F10.9 melanoma
     cells transfected with syngeneic major histocompatibility complex (MHC)
     class-I genes, modified by infection with Newcastle
     Disease virus (NDV) or modified by both treatments, was
     compared. B16-F10.9 tumor-bearing mice were treated at various stages of
     tumor growth and metastasis with irradiated, modified tumor-cell
vaccines.
     Irradiated tumor cells and H-2Db transfectants did not stimulate
     anti-tumor immunity while H-2Kb transfectants and NDV-modified F10.9
cells
     showing low and high expression of MHC class-I genes efficiently
prevented
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metastasis of small established tumors. NDV-modified parental-cell vaccines functioned optimally and improved overall survival by about 60%, also at early stages of metastasis establishment. A synergistic effect of H-2Kb expression and virus modification on rejection of micrometastases was observed in mice bearing advanced tumors. Postoperative vaccination of mice carrying multiple metastases with NDV-modified vaccines caused significant, but incomplete, **reduction** of metastatic **tumor** load. The therapeutic effect of NDV-modified tumor vaccines was dependent on multiple immune mechanisms. Depletion of CD8, CD4 or NK cells by in vivo treatment with monoclonal antibodies reversed the immunotherapeutic effects of the vaccine. Thus, tumor xenogenization and gene modification may act synergistically to vaccinate against advanced tumors, while single modalities can effectively vaccinate against metastasis at early stages of tumor growth.

L25 ANSWER 2 OF 9 MEDLINE
AU Bravard A; Hoffschir F; Sabatier L; Ricoul M; Pinton A; Cassingena R; Estrade S; Luccioni C; Dutrillaux B
TI Early superoxide dismutase alterations during SV40-transformation of human fibroblasts.
SO INTERNATIONAL JOURNAL OF CANCER, (1992 Nov 11) 52 (5) 797-801. Journal code: 0042124. ISSN: 0020-7136.
AB The expression of superoxide dismutases (SOD) 1 and 2 was studied in 4 clones of human fibroblasts after their **infection** by **simian virus** 40 (SV40), in parallel with the alterations of chromosomes 21 and chromosome 6q arms, carrying the genes that encode for SOD1 and SOD2 respectively. For all clones, a similar scheme with 2 main phases was observed for both chromosome and SOD variations. The first phase, defined as the pre-crisis phase, was characterized by chromosomal instability, but maintenance of normal numbers of chromosome 6q arms and chromosomes 21. The level of SOD2 mRNA was high, while SOD2 activity and immunoreactive protein were low. SOD1 protein and activity were decreased.
In the second phase, defined as the post-crisis phase, the accumulation of clonal chromosomal rearrangements led to the loss of 6q arms, while the number of chromosomes 21 remained normal. SOD2 mRNA level was decreased and SOD2 immunoreactive protein and activity remained low. SOD1 protein and activity increased with passages, reaching values similar to those of control cells at late passages. As in established SV40-transformed human fibroblast cell lines, good correlation was found between SOD2 activity and the relative number of 6q arms. These results allow us to reconstruct the sequence of events leading to the **decrease** of SOD2, a possible **tumor**-suppressor gene, during the process of SV40-transformation of human fibroblasts.

L25 ANSWER 3 OF 9 MEDLINE
AU Leopardi R; Vainionpaa R; Hurme M; Siljander P; Salmi A A
TI **Measles virus infection** enhances IL-1 beta but **reduces tumor** necrosis factor-alpha expression in human monocytes.
SO JOURNAL OF IMMUNOLOGY, (1992 Oct 1) 149 (7) 2397-401. Journal code: 2985117R. ISSN: 0022-1767.
AB Monocytes may play a role in the immunologic abnormalities caused by measles. The effect of measles **virus** (MV) **infection** on peripheral blood monocyte functions is poorly known. We report that MV-infected PBM have an altered pattern of IL-1 beta and TNF-alpha

production in response to stimulation with LPS and PMA in vitro. MV-infected peripheral blood monocytes produced higher amounts of IL-1 beta, whereas the production of TNF-alpha was reduced. The same effect was observed in the human monocytic cell line THP-1, which was used for RNA analysis. An increased steady-state level of IL-1 beta mRNA was observed in MV-infected cells, and the level of TNF-alpha mRNA was reduced. However, both IL-1 beta and TNF-alpha had about 50% increased transcription rate. Analysis of the mRNA stability after transcriptional block by actinomycin D showed that the TNF-alpha mRNA had a reduced half-life in MV-infected cells (about 30 vs 80 min in uninfected cells), whereas IL-1 beta mRNA stability was similar in uninfected and MV-infected cells. These results indicate that MV infection disturbs the immunoregulatory network by interfering with the monocyte functions.

L25 ANSWER 4 OF 9 MEDLINE
AU Moore M; Teresky A K; Levine A J; Seiberg M
TI p53 mutations are not selected for in simian virus 40 T-antigen-induced tumors from transgenic mice.
SO JOURNAL OF VIROLOGY, (1992 Feb) 66 (2) 641-9.
Journal code: 0113724. ISSN: 0022-538X.
AB Many diverse tumors contain cells that select for mutations at the p53 gene locus. This appears to be the case because the p53 gene product can act as a negative regulator of cell division or a **tumor** suppressor. These mutations then **eliminate** this activity of the p53 gene product. The **simian virus** 40 (SV40) large T antigen binds to p53 and acts as an oncogene to promote cellular transformation and initiate tumors. If the binding of T antigen to the p53 protein inactivated its tumor suppressor activity, there would be no selection pressure for p53 mutants to appear in tumors. To test this idea, transgenic mice that carried and expressed the SV40 large T-antigen gene were created. Expression of the T antigen was directed to the liver, using the albumin promoter, and the choroid plexus, using the SV40 enhancer-promoter. A large number of papillomas (indicated in parentheses) of the choroid plexus (14), hepatocellular carcinomas (5), liver adenomas (10), and tumors of clear-cell foci (5) were examined for mutant and wild-type p53 genes and gene products. In all cases, the tumor extracts contained readily detectable T-antigen-p53 protein complexes. A monoclonal antibody specifically recognizing the wild-type p53 protein (PAb246) reacted with p53 in every tumor extract. A monoclonal antibody specifically recognizing mutant forms of the p53 protein (PAb240) failed to detect p53 antigens in these extracts. Finally, p53 partial cDNAs were sequenced across the regions of common mutations in this gene, and in every case only the wild-type sequence was detected. These results strongly support the hypothesis that T antigen inactivates the wild-type p53 tumor-suppressing activity and there is no need to select for mutations at the p53 locus.

L25 ANSWER 5 OF 9 MEDLINE
AU Giese N A; Neary K E; Levine N; Lindell T J; Duffy J J
TI Inhibition by retinoic acid of murine retrovirus-induced cellular transformation and tumor formation.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1985 May) 74 (5) 1135-44.
Journal code: 7503089. ISSN: 0027-8874.

AB The effect of all-trans-retinoic acid (RA) on cellular transformation and on tumorigenicity of retrovirally transformed cells was investigated. RA treatment of NRK and NIH/3T3 cells transformed by BALB/c murine sarcoma virus (MuSV), Kirsten murine sarcoma **virus** (K-MuSV), and **simian** sarcoma **virus** resulted in a significant reduction in anchorage-dependent growth of only K-MuSV-transformed NRK cells. A 62% reduction in cell number was observed at 10(-5) M RA. In contrast, anchorage-independent growth induced by each of the viruses tested was suppressed by RA. Balb/cMSV3T3 cells showed the greatest level of sensitivity with a significant reduction in anchorage-independent growth occurring at 10(-9) M RA. The level of cytoplasmic retinoic acid-binding protein (CRABP) was determined in both parent and transformed cell lines. CRABP was present at a high level in all 3T3 cell types but was absent in all NRK cell lines. For testing the antineoplastic activity of RA in vivo, Balb/cMSV3T3 cells were injected intradermally into nude mice. Subsequent treatment of the tumor sites of these animals by topical application of RA resulted in a significant **reduction** in both **tumor** incidence and tumor size, confirming the in vitro results. Analysis of the level of v-onc mRNA revealed that inhibition of retroviral transformation by RA was not due to a decrease in transcription of the v-onc genes.

L25 ANSWER 6 OF 9 MEDLINE
AU Ohtaki S
TI Suppressive effects on simian virus 40-induced oncogenesis of several immunosuppressive agents and hormonal modifications applied during the latent period.
SO CANCER RESEARCH, (1978 Dec) 38 (12) 4698-710. Ref: 47
Journal code: 2984705R. ISSN: 0008-5472.
AB The long latent period required for tumor induction with **Simian virus** 40 (SV40) in the subcutis of hamsters can be used to investigate whether host factor(s) participate in oncogenesis. Several treatments were applied during this period, and the results were compared with those of the same treatment applied in another series of experiments, homologous SV40 tumor grafting in hamsters. The results obtained were as follows: (a) the latent period for SV40 tumor induction in the female was shorter than that in the male; tumor development was delayed significantly by oophorectomy but was little affected by orchiectomy. Tumor development was markedly delayed in animals of both sexes by estrone given at birth but was accelerated by testosterone given in the adult male; (b) by each of these hormonal modifications, growth of transplanted SV40 tumors was influenced in a different way from that of tumor induction; (c) immunosuppressive treatments, such as thymectomy, administration of antilymphocyte sera, cyclophosphamide, or cortisone acetate delayed and **decreased tumor** development when applied in the latent period, and the degree or pattern of this effect varied from one procedure to another, depending on the sex and age of the animals; (d) in contrast, tumor growth was markedly accelerated in thymectomized or cortisone-treated hosts irrespective of sex. The different and almost reverse effect of the same procedure in the two phases of tumorigenesis may indicate two discriminating mechanisms operating in the host during these phases. This different effect may be due to virtual absence of any "mature" neoplastic cell in the latent period, except for a few weeks before the appearance of a palpable tumor. These results suggest that the long period of latency may be spent to complete SV40-induced neoplastic

conversion of cells, receiving some help by host factors.

L25 ANSWER 7 OF 9 MEDLINE
AU Henriksen O; Law L W; Appella E
TI Quantitative in vivo studies of soluble simian virus 40 tumor-specific transplantation antigens of the mouse.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1977 Jun) 58 (6) 1785-8.
Journal code: 7503089. ISSN: 0027-8874.
AB Quantitative studies have been performed on the immunogenicity of a membrane-bound antigen of a **simian virus** 40 (SV40) -induced sarcoma in syngeneic BALB/c mice and of subcellular fractions derived from this tumor. The objectives of the investigation were: a) to develop a quantitative in vivo assay of the tumor-specific transplantation antigen (TSTA) and b) to compare the distribution of histocompatibility antigens, H-2, with that of the SV40 TSTA during several fractionation steps. The immunogenicity of the TSTA-containing fractions was assessed from dose-response curves relating tumor size and the amount of protein used for immunization. After digestion of the tumor cell membranes with a limited amount of papain, H-2 as well as TSTA were present in a soluble form. A single immunization with only 2 microng of the solubilized TSTA **reduced** the **tumor** size by 70% compared to that in nonimmunized control animals. The results of several fractionation steps suggest that H-2 and the TSTA are not tightly associated in the solubilized immunogenic material.

L25 ANSWER 8 OF 9 MEDLINE
AU Kuzumaki N; Kobayashi H
TI Reduced transplantability of syngenic mouse tumors superinfected with membrane viruses in nu/nu mice.
SO TRANSPLANTATION, (1976 Dec) 22 (6) 545-50.
Journal code: 0132144. ISSN: 0041-1337.
AB Transplantability of mouse tumors superinfected with various kinds of membrane viruses was investigated in syngeneic hosts. Methylcholanthrene-induced fibrosarcomas in BALB/c mice, Meth A, and in C57BL/6 mice, BMT-, superinfected with Friend lymphatic leukemia virus in mice given neonatal injection of the virus, grew more slowly than uninfected tumors. The retardation of growths was not observed in mice that had been given injections of the virus at birth. Similarly, Meth A and a hepatoma in C3H/He mice, MH134, superinfected with Moloney murine sarcoma virus in nu/nu mice, had reduced their transplantability in respective syngeneic mice. Further, Meth A and MH134 superinfected with endogenous rat leukemia **virus** and human **measles virus**, respectively, in nu/nu mice also showed reduced transplantability, and some of the former were actually rejected by normal syngeneic hosts. On the other hand, the reduced transplantability was not found in irradiated mice, suggesting that the phenomenon was due to immunological events. However, a myelogenous leukemia in C57BL/6 mice, C1498, superinfected with Moloney sarcoma virus in nu/nu mice grew like uninfected **tumor** and did not show **reduced** transplantability at all.

L25 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS
IN Russell, James; Cattaneo, Roberto; Peng, Kah-Whye; Schneider, Urs; Murphy, Anthea L.
TI Therapeutic methods and compositions using viruses of the recombinant Paramyxoviridae family
SO PCT Int. Appl., 102 pp.

CODEN: PIXXD2

AB The invention relates to compns. and methods for treating a patient having a **tumor** in order to **reduce tumor** size, comprising administering to the patient a replication-competent **Paramyxoviridae** virus comprising two or more of a) a nucleic acid sequence encoding a heterologous polypeptide, wherein upon administration the heterologous polypeptide is detectable in a biol. fluid of the patient, and detection of the heterologous polypeptide is indicative of **Paramyxoviridae** virus growth in the patient and **redn.** in **tumor** size; b) a recombinant F protein, H protein, or M protein of **Paramyxoviridae** virus that increases fusogenicity of virus with cells; c) a nucleic acid sequence encoding a cytokine; and d) a **Paramyxoviridae** virus that is specific for cells of the tumor.

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L25 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2001:228648 CAPLUS
DN 134:256837
TI Therapeutic methods and compositions using viruses of the recombinant Paramyxoviridae family
IN Russell, James; Cattaneo, Roberto; Peng, Kah-Whye; Schneider, Urs; Murphy, Anthea L.
PA Mayo Foundation for Medical Education and Research, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
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PI WO 2001020989	A1	20010329	WO 2000-US26116	20000922
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EP 1217891	A1	20020703	EP 2000-965349	20000922
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WO 2000-US26116	W	20000922		

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